Lead and Compounds

CAS Registry Number: 7439-92-1

I. Physical and Chemical Properties

Description	Bluish-gray metal
Molecular formula	Pb
Molecular weight	207.2
Air concentration conversion	Not applicable

II. Overview

Epidemiological studies have shown that at low lead levels neurodevelopmental effects occur in children (Bellinger *et al*., 1984a, b; McMichael *et al*., 1994; Needleman *et al*., 1996). While the CDC and the U.S. EPA have identified a blood lead concentration of 10 µg/dL as the level of concern, no threshold levels for adverse effects have been identified for inorganic lead. To correlate blood lead with air lead levels, OEHHA developed slope factors of 1.8 µg/dL $(\mu g/m^3)^{-1}$ for adults and 4.2 µg/dL $(\mu g/m^3)^{-1}$ for children. These slope factors reflect the higher rate of lead uptake in children compared to adults.

Data from the National Health and Nutrition Examination Survey (NHANES III) indicate that approximately 5.9% of children one to two years of age already have blood lead levels exceeding 10 µg/dl. At an ambient level of 0.011 $\mu g/m^3$, an additional 4,560 of the 1.2 million one and two year old children will move above the 10 µg/dL threshold compared to zero air lead (extrapolated from Table 2). At an air lead concentration equivalent to the current ambient air standard of 1.5 $\mu g/m^3$, more than 45% of children aged one and two would have blood lead levels above the CDC guideline of 10 µg/dL according to the aggregate model employed by OEHHA. Thus while the state-wide ambient lead levels in 1998 were substantially below this level (0.011 $\mu g/m^3$; CARB, 2000a), we are concerned that children exposed to locally high emissions of lead from stationary sources are at substantial risk for adverse health effects.

III. Principal Sources of Exposure

At current ambient lead concentrations, airborne lead is on average a minor contributor to a child's overall lead exposure. The major airborne exposures to environmental lead appear to be localized sources including deterioration of lead-based painted surfaces, lead that has accumulated in dust and soil, and near point sources of air emissions. Deposition of particulate lead on food and water is another indirect route of exposure to airborne lead. The ambient air lead concentration in California in 1998 was 0.011 $\mu g/m^3$ as reported by the California Ambient Toxics Monitoring Network (CARB, 2000a). Annual lead emissions from stationary sources in 1998 reported as part of the Air Toxics Hotspots program were 233,797 lbs/yr (CARB, 2000b)

IV. Potential for Differential Effects

A large and growing body of evidence indicates that children are more sensitive to the neurotoxic effects of lead than are adults. Because low levels of lead exposure have been associated with developmental delays and decrements in intelligence, short term memory, perception integration, visual motor functioning, and behavior in children (Bellinger *et al*., 1984a, b; Needleman *et al*., 1996; Needleman and Gatsonis, 1990), lead is considered a priority chemical for evaluation of potential differential effects on infants and children.

A. Summary of Key Human Studies

Lead has been associated with adverse reproductive and developmental outcomes. Maternal blood lead levels of 10 to 15 µg/dL have been associated with pre-term delivery and low birthweight. Based on data from NHANES, Schwartz *et al*. (1986) reported small but significant reductions in early childhood growth with no apparent threshold across the range of 5-35 µg/dL. Blood lead levels of 10 µg/dL and below have been associated with decreased hearing acuity (Schwartz and Otto, 1987). Pre- and postnatal lead exposure have been negatively associated with measures of intelligence, such as IQ in infants and young children (OEHHA, 1997). These effects were noted at blood levels of 10-20 µg/dL and lower. Indeed, Lanphear *et al*. (2000) used NHANES III data on children 6-16 years of age and found an inverse association between cognitive functions measured on the Wide Range Achievement Test-Revised (WRAT-R) (reading, math, block design, digit span) and blood lead concentration in the range of <2.5 to <10 µg/dL. Significant inverse correlations were found between blood lead levels as low as < 5.0 µg/dL and decrements in math ($p = 0.03$) and reading ($p < 0.001$) (Table 3).

Lead's neurodevelopmental effects, observed at low to moderate exposure levels (30 µg/dL and below) include: decreased intelligence, short-term memory loss, reading and spelling underachievement, impaired visual motor functioning, poor perception integration, disruptive classroom behavior, and impaired reaction time (Bellinger *et al*., 1984a, b; Needleman *et al*., 1996).

Needleman *et al*. (1979), using lead levels in the teeth of first and second graders, found a significant association between increased dentine lead level and decrements in intelligence quotient (IQ). The association was still evident when the children were tested 5 and 11 years later (Bellinger *et al*., 1984b; Needleman *et al*., 1990). Needleman and Gatsonis (1990) undertook a meta-analysis of the published IQ-blood lead studies. The results suggested that each 1 µg/dL increase of blood lead results in a 0.24 point decrease in IQ.

Large, long-term, prospective studies were conducted in Boston, Cincinnati, and Port Pirie, Australia. One of the larger cohorts studied, from Boston, Massachusetts, included several hundred middle and upper-middle class children followed from birth to 10 years of age (Bellinger *et al*., 1984a, 1985, 1991, 1992; Stiles and Bellinger, 1993). These studies have consistently found an association between blood lead and IQ among different age cohorts. Among the more important findings are those of older children since their IQs may be better characterized in the standardized tests. For example, at age 10 years, the children were examined again using the Wechsler Intelligence Scale for Children-Revised

(WISC-R), a measure of cognitive function, as well as the Kaufman Test of Educational Achievement (KTEA) (Bellinger *et al*., 1992; Stiles and Bellinger, 1993). Higher levels of blood lead at 24 months of age were associated with significantly lower scores on FSIQ (full scale IQ) and verbal IQ. The authors observed a decrease of almost 6 points on FSIQ and 9 points on KTEA Battery Composite score for each 10 µg/dL increase in lead level at 24 months of age. These estimates include adjustments for maternal age, race, marital status, number of residence changes and home environment. Visual inspection of the results and analysis of an earlier data set (Schwartz, 1993) suggest a continuous response across the entire range of blood lead levels and the lack of any threshold. Children from lower socioeconomic status appeared to be more sensitive to effects at lower blood lead concentrations. A more recent study found that lead impacted high school classroom behavior (Needleman *et al*., 1996). Therefore, evidence from these studies suggests that both prenatal and postnatal exposure may be associated with adverse impacts on cognitive performance with effects from postnatal exposure persisting to at least 10 years of age. The effects of later postnatal exposure seem to be strongest.

Other large prospective studies of lead and neurodevelopment involve cohorts of inner-city children in Cincinnati, Ohio and children in Port Pirie, South Australia (McMichael *et al*., 1994). Although there are differences in socioeconomics and demographics, experimental techniques, statistical models, and patterns of exposure among the three large cohort studies, their findings are consistent. Among the more relevant findings, changes in IQ at ages 6 to 10 are associated with blood lead measured either cumulatively over several years or in a single year. In addition, the magnitudes of effect per µg/dL are similar among both the prospective and cross-sectional studies. Many of these studies report mean blood concentrations near 10 µg/dL.

Several meta-analyses have been conducted of the prospective studies relating low-level blood lead exposures to neurodevelopmental effects in young children. Researchers with the CDC (Thacker *et al*., 1992) reviewed 35 prenatal and early postnatal prospective cohort studies and concluded that the weight of evidence suggested an inverse relationship between lead and the intelligence of children. Pocock *et al*. (1994) reviewed several types of study to quantify the relationship between lead and IQ, including the WISC-R. The analysis concluded that for postnatal blood lead, both the cross-sectional and prospective studies indicate a significant inverse association between blood lead and IQ. In addition, Schwartz (1994) conducted meta-analyses of both longitudinal and cross-sectional neurodevelopmental studies and concluded that the two study designs were capturing similar effects.

To provide an estimate and range of risk, OEHHA performed a simplified meta-analysis (Hedges and Olkin, 1985) of cohort studies conducted in children older than 5 years. This age group was used because it is likely to provide the most accurate assessment of the impact of blood lead. Estimates of the mean effect were derived by weighting each of the regression coefficients by the inverse of its variance. This generated a mean decrease of 0.33 IQ points per µg/dL blood lead with a 95% confidence interval of 0.32 to 0.34 (Table 1). Thus, this central estimate suggests that a 1 µg/dL increase in postnatal blood lead is associated, on average, with a 0.33 point decrease in FSIQ. This level is close to the range of estimates derived from the earlier meta-analyses, cited above. OEHHA used this value in its identification of lead and lead compounds as a toxic air contaminant (OEHHA, 1997).

In addition to the general effect magnitude, the overall population-level impact of IQ is also important to consider. Grant and Davis (1989) have demonstrated that, if one shifts down a normal distribution of IQ scores (mean=100, standard deviation=16) by 4 points, the number of children scoring 80 or below increases by 50%. The impact of such a shift applies across the entire distribution of scores, reducing the number of children who score above the norm as well as increasing the number scoring well below the norm. Thus, while a 4-point IQ loss might not have much impact on an individual child, this decrease could have a significant public health impact in a community. Similarly, a shift of 3.3 points would increase the percent of children scoring 80 or below from 10.56% to 14.74%, a 39.5% increase.

Based on current information it is not possible to identify a clear threshold blood lead level associated with adverse health effects in humans. The level of concern where human neurodevelopmental effects are seen in children exposed either prenatally or postnatally has been identified at 10 µg/dL. However, as the evidence continues to grow, it is possible that future levels of concern may drop below 10 µg/dL. The consistency of findings lends strong support to the conclusion that neurodevelopmental effects are causally associated with blood lead, and that the CDC level of concern of 10 µg/dL is a reasonable action level.

B. Summary of Key Animal Studies

Many of the neurological and cardiovascular effects noted in humans have also been observed in experimental animals. Lead in the diet of pregnant mice resulted in marked reductions in fertility and retarded growth of pups. Embryotoxicity and fetotoxicity have been observed and the toxic effects depend on the day of gestation when lead was administered (Domingo, 1994; Ronis *et al*., 1998). Early postnatal lead exposure in rats causes long-lasting cholinergic deficits (Bielarczyk *et al*., 1994; 1996). Prolonged deficits in learning behavior have been observed in monkeys exposed to lead *in utero* (Newland *et al*., 1996). The enormous number of studies of the toxicity of lead in animals supports that observed in humans (ATSDR, 1999; OEHHA, 1997). The neurotoxic effects seen following postnatal exposure of experimental animals include altered neurochemistry, histopathology, delay in development of reflexes, poor performance in learning tasks, and other behavioral measures.

V. Additional Information

A. Other Toxicity

Anemia in adults has been reported at blood lead levels of 40-60 µg/dL (Baker *et al*., 1979), and in children at 30-40 µg/dL (Schwartz *et al*., 1990). Increased blood pressure in adults has been reported at blood lead concentrations as low as 10 µg/dL.

B. Regulatory Background

The current California Ambient Air Quality Standard is 1.5 $\mu g/m^3$ averaged over one month. A cancer unit risk factor of 1.2 E-5 $(\mu g/m^3)^{-1}$was calculated for lead by OEHHA (1997) from rat kidney tumor incidence data (Azar *et al*., 1973).

The CDC and others have concluded that blood lead concentrations at or near 10 µg/dL present a public-health risk to infants, children and pregnant women (CDC, 1991; U.S. EPA, 1990; NRC, 1993). OEHHA concurred with this level of concern in our TAC document (OEHHA, 1997). This blood lead level is the CDC level of concern for communities as a whole, as well as for individuals.

VI. Conclusions

The neurotoxicity of lead has been well-characterized, and children are a sensitive subpopulation for this effect. Although average ambient concentrations are low, there are many children with blood lead levels above 10 µg/dl, the level of concern for effects in children. In addition, there are significant emissions of lead from stationary sources reporting under the Air Toxics Hot Spots program, and near-source exposures will be higher than ambient averages. Additional exposure, either ambient or near-source, pushes more children above the level of concern. Furthermore, new studies indicate impacts in children at blood lead levels below 10 µg/dl. For all these reasons, therefore, OEHHA has placed lead in Tier 1.

Table 1. Regression Coefficients Indicating Change in IQ per 1.0 µg/dL Increase in Blood Lead for Crude and Adjusted Models in Prospective Studies at Later Ages

Crude Model:		
Study	Intelligence Measure	Coefficient (s.e.)
Boston[a]	WISC-R (FSIQ)	-0.71 (0.25)
Cincinnati[b]	WISC-R (FSIQ)	-0.58 (0.13)
Adjusted Model:		
Study	Intelligence Measure	Coefficient (s.e.)
Boston[c]	WISC-R (FSIQ)	-0.58 (0.21)
Cincinnati[d]	WISC-R (FSIQ)	-0.33 (0.14)
Port Pirie[e, f]	WISC-R (FSIQ)	-0.24 (0.12)
Meta-Analyses:		
Study	Intelligence Measure	Coefficient (s.e.)
Needleman and Gatsonis[g]	Varied	-0.25 (0.04)
Schwartz[h]	Varied	-0.24 (0.04)
OEHHA[I]	WISC-R (FSIQ)	-0.33

a) Blood lead at age 2, WISC-R at age 10, unadjusted analysis.
b) Mean blood lead at age 6, WISC-R at age 6.5.
c) Adjusted for HOME score at 10 years, maternal age, race, marital status, and number of residence changes prior to 57 months.
d) Adjusted for HOME score, maternal IQ, birth weight, birth length, gender, and cigarette consumption during pregnancy.
e) Averaged blood lead at ages 0-4, linearized using PbB mean of 19.59, WISC-R at age 7.
f) Adjusted for sex, parent's level of education, maternal age at delivery, parental smoking status, SES, HOME score, birth weight, birth order, feeding method, duration of breast feeding and whether or not child's parents were still living together.
g) Meta-analysis of six cross-sectional studies of blood lead and intelligence.
h) Meta-analysis using same six cross-sectional studies and one additional prospective study by Bellinger *et al*. (1991).
i) Meta-analysis using the three above "Adjusted Models."

Sources: *Stiles and Bellinger (1993); Bellinger et al. (1992), Dietrich et al. (1993), Baghurst et al. (1992), Needleman and Gatsonis (1990), Schwartz (1993), OEHHA (1997)*

Table 2. Association Between Ambient Air Lead and the Expected Percent of One and Two Year Old Children Equal to or Above 10 mg/dL Blood Lead.

	GM = 3.14 *** GSD = 2.1	GM = 3.14 GSD = 1.8	GM = 2.5 GSD = 1.8
Average Air Lead Concentration ($\mu g/m^3$)	Percent ≥ 10 µg/dL	Percent ≥ 10 µg/dL	Percent ≥ 10 µg/dL
0.011*	4.3	0.95	0.79
0.055**	5.9	2.4	1.0
0.10	6.9	3.0	1.3
0.25	10.6	5.7	3.0
0.50	17.6	12.0	8.0
1.00	32.2	28.1	22.9
1.50	45.6	44.4	39.6

* California ambient air lead concentration for 1999 (CARB 2000a).

** National average air lead concentration during the period of data collection of NHANES III, Phase 2. Calculation assumes that baseline non-air sources of lead exposure including paint, household dust, soil, pottery, and tap water are constant.

*** Geometric Mean (GM) = 3.14 and Geometric Standard Deviation (GSD) = 2.1 are taken from NHANES III, Phase2, and represent the blood lead distribution for children ages one and two (Pirkle *et al*., 1998).

Table 3. Adjusted Coefficients of Blood Lead Concentration from Multiple Regression Analyses of Cognitive Function Scores at Various Cut-offs for Children and Adolescents, 6 to 16 Years of Age, NHANES III. Coefficient (std errors) Represents the Decrement Associated with Each 1 µg/dL Increase in Blood Lead Concentration.

Variable	Total Sample n = 4,853	< 10 µg/dL n = 4,681	< 7.5 µg/dL n = 4,526	< 5.0 µg/dL n = 4,043	< 2.5 µg/dL n = 2,467
Math	-0.70 (0.17) (p < 0.001)	-0.89 (0.32) (p = 0.008)	-1.06 (0.39) (p = 0.01)	-1.06 (0.48) (p = 0.03)	-1.28 (0.98) (p = 0.20)
Reading	-0.99 (0.19) (p < 0.001)	-1.44 (0.30) (p < 0.001)	-1.53 (0.31) (p < 0.001)	-1.66 (0.36) (p < 0.001)	-1.71 (0.93) (p = 0.07)
Block Design	-0.10 (0.04) (p = 0.009)	-0.13 (0.06) (p = 0.03)	-0.11 (0.06) (p = 0.04)	-0.05 (0.07) (p = 0.45)	-0.08 (0.22) (p = 0.72)
Digit Span	-0.05 (0.22) (p = 0.04)	-0.08 (0.04) (p = 0.03)	-0.09 (0.05) (p = 0.11)	-0.09 (0.07) (p = 0.20)	-0.25 (0.17) (p = 0.17)

Adjusted for gender, ethnicity, poverty index, parent education and iron status.

Source: *Lanphear et al. (2000) Public Health Rep. 115;521-9.*

VI. References

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